

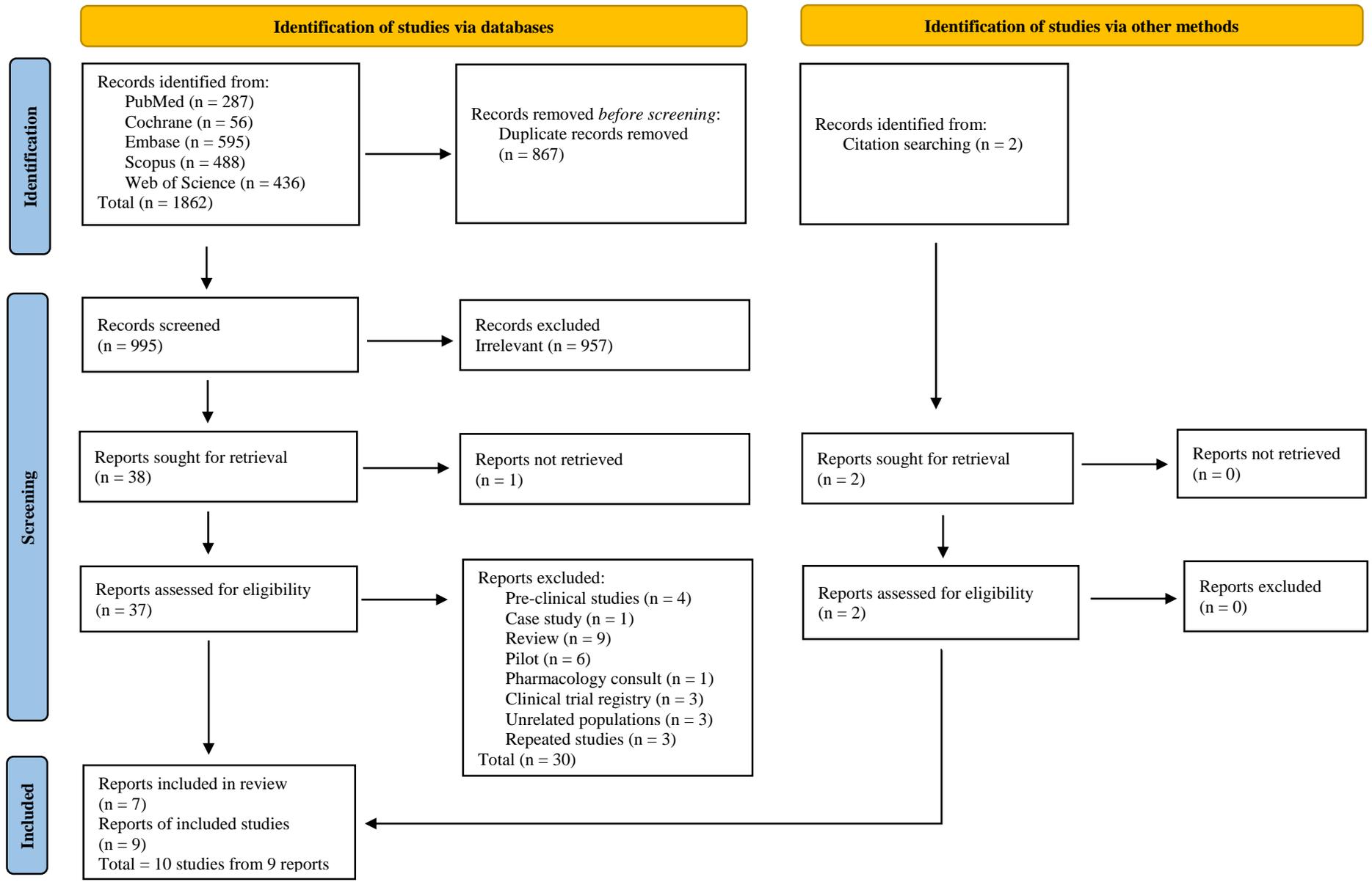
Supplementary Material

The Effects of Medium Chain Triglyceride for Alzheimer’s Disease Related Cognitive Impairment: A Systematic Review and Meta-Analysis

Supplementary Table 1. Comprehensive search strategy employed in each database.

Source	Search Strategy	Hits retrieved
PubMed	("neurocognitive disorders"[Mesh] OR "dementia"[All Fields] OR "alzheimer"[All Fields] OR "amyloid"[Mesh] OR "amyloid"[All Fields]) AND ("cocos"[Mesh] OR "coconut oil"[Mesh] OR "coconut"[All Fields] OR "coconut oil"[All Fields] OR "ketone bodies"[Mesh] OR "ketone bodies"[tiab] OR "medium chain triglycerides"[tiab])	287
Cochrane	<ol style="list-style-type: none"> 1. MeSH descriptor: [Cocos] explode all trees 2. MeSH descriptor: [Coconut oil] explode all trees 3. MeSH descriptor: [Ketone bodies] explode all trees 4. “coconut oil” or “coconut” 5. (“ketone bodies”):ti,ab,kw 6. (“medium chain triglycerides”): ti,ab,kw 7. #1 or #2 or #3 or #4 or #5 or #6 8. MeSH descriptor: [Neurocognitive disorders] explode all trees 9. MeSH descriptor: [Amyloid] explode all trees 10. alzheimer or dementia or amyloid 11. #8 or #9 or #10 12. #7 and #11 13. Extracted only trials 	56
Embase	<ol style="list-style-type: none"> 1. ‘neurocognitive disorders’/exp 2. ‘dementia’ 3. ‘alzheimer’ 4. ‘amyloid’ 5. or/1-4 6. ‘cocos’/exp 7. ‘coconut oil’/exp 8. ‘ketone bodies’/exp 9. ‘coconut’ 10. ‘coconut oil’ 11. ‘medium chain triglycerides’:ab,ti 12. ‘ketone bodies’:ab,ti 13. or/6-12 14. #5 and #13 	595
Scopus	(TITLE-ABS-KEY ("neurocognitive disorders" OR dementia OR alzheimer OR amyloid) AND TITLE-ABS-KEY (cocos OR "coconut oil" OR "ketone bodies" OR coconut OR "medium chain triglycerides"))	488
Web of Science	<ol style="list-style-type: none"> 1. TOPIC: ("neurocognitive disorders") <i>OR</i> TOPIC: (dementia) <i>OR</i> TOPIC: (alzheimer) <i>OR</i> TOPIC: (amyloid) 2. TOPIC: (cocos) <i>OR</i> TOPIC: ("coconut oil") <i>OR</i> TOPIC: (coconut) <i>OR</i> TOPIC: (ketone bodies) <i>OR</i> TOPIC: ("medium chain triglycerides") 3. #1 and #2 	436

Supplementary Figure 1. A flowchart summary of the systematic literature search process.



Supplementary Table 2. Detailed description of general cognitive function test.

Test	Subtests	Description	Scoring
ADAS-Cog		After conducting the ADAS-Cog, the examiner adds up the points for the errors in each of the subtests of ADAS-Cog to obtain a final score. Hence, the higher the score, the more severe the cognitive impairment in the subject undertaking the test.	
	Word Recall	Subject is given a list of ten words to be read out. Subject is then tasked to verbally recollect as many words as possible. This task is repeated three times.	Score is given based on the average number of words not recollected; each word is given a score of 1 and a range of score from 0 to 10 can be awarded.
	Language	Examiner engages in a ten-minute conversation with subject, to assess language ability. The remaining tasks are then presented subsequently.	The quality of speech is determined by the examiner based on a global rating; a range of score from 0 to 5 can be awarded.
	Comprehension of Spoken Language	Examiner assesses subject's level of comprehension during the ten-minute conversation.	Based on the assessment by the examiner, and a range of score from 0 to 5 can be awarded.
	Word Finding Difficulty	The examiner assesses whether subject is having difficulty in finding words to express themselves during the ten-minute conversation.	Based on the assessment by the examiner, and a range of score from 0 to 5 can be awarded.
	Naming Objects and Fingers	Subject is tasked to name the five fingers on their dominant hand. Subject is also tasked to name the following twelve objects: flower (plastic), bed (doll house furniture), whistle, pencil, rattle, mask, scissors, comb, wallet, harmonica, stethoscope, and tongs	The number of fingers and objects correctly named; a range of score from 0 to 4 can be awarded.
	Commands	Subject is given 5 commands to perform. Commands are in sequential order from step one to step 5.	Score is given based on the highest number of step subject can perform correctly; and a range of score from 0 to 5 can be awarded.
	Constructional Praxis	Subject will be shown the following shapes: circle, two overlapping rectangles, rhombus and cube); subject is tasked to copy the shapes on a piece of paper.	Score is given based on correctly drawn shapes, where each shape is given a score of 1; a range of score from 0 to 5 can be awarded.
	Ideational Praxis	Subject is tasked to act out the following scenario of mailing a letter to themselves: fold letter, put letter in envelope, seal envelope, address envelope, and put a stamp on the envelope.	Score is given based on whether subject is experiencing difficulty in performing the five components; a range of score from 0 to 5 can be awarded.
	Orientation	Subject needs to respond to the following: day of the week, date, month, year, season, time of day, place and person	Score of 1 is given for each correct response; a range of score from 0 to 8 can be awarded.
Word Recognition	Subject is given a list of twelve words to be read out, which are later combined with twelve new words. Subject is then tasked to pick out words seen previously. This task is repeated three times.	Score is given based on the average number of words correctly recognized; each word is given a score of 1 and a range of score from 0 to 12 can be awarded.	

	Remembering Test	The examiner assesses the frequency which subjects require reminder of the instructions for the Word Recognition test.	Based on the assessment by the examiner, a range of score from 1 to 5 can be awarded.
ADCS-CGIC	Examiner is to interview the subject before the informant on the following: 1. Recent medical history 2. The general appearance of subject		ADCS-CGIC is an assessment of disease progression administered at baseline and post-treatment. The interview is conducted separately on the subject and informant; subject is interviewed before the informant. After completing the interviews, based on the examiner's own judgement, the clinical impression of change is recorded on a 7-point Likert-type scale: 1. Marked improvement 2. Moderate improvement 3. Minimal improvement 4. No change 5. Minimal worsening 6. Moderate worsening
	<i>Mental/Cognitive State</i> Examiner is to interview the subject before the informant on the following: 1. Alertness and of subject 2. Memory, including delayed and immediate memory 3. Communication ability of subject 4. Processing skills of subject 5. Subjects' behavior in situations requiring judgement.		
	<i>Behavior</i> Examiner is to interview the subject before the informant on the following: 1. The organization and appropriateness of thoughts of subject 2. Is subject experiencing any signs of hallucinations or delusions? 3. The behavior and mood of subject 4. The sleep and appetite of subject 5. The motor abilities of subject		
	<i>Functioning</i> Examiner is to interview the subject before the informant on the following: 1. The ability of subject to carry out self-grooming activities by themselves and complex activities such as handling finances, conducting household chores, driving etc. 2. The ability of subject to engage in conversations with people around him/her		
MMSE/MEC/ Mec-Lobo	The MEC/Mec-lobo is a validated translation of the Mini-Mental State Examination (MMSE) into Spanish. Individual domains of cognition measured in the test includes orientation, calculation concentration, fixation, memory and language construction.		
	Orientation to Time	Subject needs to respond to the following: day of the week, date, month, year and season.	Score of 1 is given for each correct response; a range of score from 0 to 5 can be awarded.
	Orientation to Place	Subject needs to respond to questions regarding their current setting.	A range of score from 0 to 5 can be awarded.
	Repetition/ Registration	Examiner will read out three unrelated words: apple, penny, table, pausing for a second after each word. Subject is then tasked to repeat the three words.	Score is given for each correct answer; subject can obtain a range of score from 0 to 3. The order of recall is irrelevant, but phonemic or paraphasic errors should be penalized.
	Attention and Calculation	Subject will be asked to subtract 7 from 100, followed by another 7 for five cycles	Score is given for each correct answer; a range of score from 0 to 5 can be awarded.

	<u>Alternative</u> Subject will be asked to spell a word forward, and mistakes will be corrected; subject will then have to spell the same word backwards.	<u>Alternative</u> Score is given for each letter spelled in the correct order backwards, one point is removed for each extra or missing letter; a range of score from 0 to 5 can be awarded.
Recall	Subject is tasked to recall the three words given by the examiner early without prompting or reminders.	Score is given for each correct answer; a range of score from 0 to 3 can be awarded.
Naming	Examiner will point to two objects, to which subject is required to name them. Examples of objects: pen/pencil and watch or glasses and keys	Score is given for each correctly named object; a range of score from 0 to 2 can be awarded.
Repetition	Examiner will read out the following sentence with clear articulation “no ifs ands or buts”, pausing after each word. Subject is tasked to repeat the sentence above.	Score is given when all the words are clearly articulated in the correct order.
Comprehension	Subject will be given verbal instructions clearly and loudly to which they are tasked to follow. No prompting or reminders to be given to subjects.	Score is given for each step performed correctly; a range of score from 0 to 3 can be awarded.
Reading	Subject will be given a paper with ‘CLOSE YOUR EYES’ written on it. Subject is tasked to read the instruction and then follow the instruction.	Score is given if subject closes his/her eyes.
Writing	Subject is tasked to write a sentence on a piece of paper. Examiner may prompt subject with topics.	Score is given if sentence written contains a subject and verb, and is comprehensible.
Drawing	Subject will be shown two clearly drawn intersecting pentagons; subject is tasked to copy the diagram on a piece of paper.	Score is given if the correct shape is drawn.
MoCA	The Montreal Cognitive Assessment (MoCA) is used for screening of cognitive dysfunction which can be administered in 10 minutes. A maximum score of 30 can be obtained for MoCA and lower score indicates more severe cognitive dysfunction.	
Visuospatial/ Executive	<u>Task 1</u> Subject is tasked to join the bubbles in alternating numbers and letters in the correct sequence.	<u>Task 1</u> A maximum score of 1 is given if subject can correctly join the bubbles in the correct order.
	<u>Task 2</u> Subject is tasked to copy a cube on the piece of paper.	<u>Task 2</u> A maximum score of 1 is given if subject can correctly copy the cube.
	<u>Task 3</u> Subject is tasked to draw a clock (ten past eleven).	<u>Task 3</u> Score is given based on the accuracy of the contour, numbers and hands of the clock. A range of score from 0 to 5 can be awarded.

Naming	Subject will be shown three pictures of the following animals: lion, rhinoceroses and camel. Subject is to name them.	Score of 1 is given for each correctly named animal; a range of score from 0 to 3 can be awarded.
Memory	Examiner will read out the following words: face, velvet, church, daisy, red. Subject is tasked to repeat the list of words. This task is repeated three times.	No score is given for this test.
Attention	<u>Task 1</u> Examiner will read out two lists of digits, pausing for a second after each digit. Subject is then required to repeat the digits in the forward order. Subject are also required to repeat another list of digits in the backward order.	<u>Task 1</u> Score is given when the correct order is repeated; a range of score from 0 to 2 can be awarded.
	<u>Task 2</u> Examiner will read out a list of letters and subject must tap with his/her hand when they hear the letter 'A'.	<u>Task 2</u> No score will be awarded if subject commits more than or equals to 2 errors.
	<u>Task 3</u> Subject will be asked to subject 7 from 100, followed by another 7, and continue for a total of 5 subtractions.	<u>Task 3</u> Scores are given based on the following correct response: 1. 3 points – 4 or 5 correct subtractions 2. 2 points – 2 or 3 correct subtractions 3. 1 point – 1 correct subtraction 4. 0 points – 0 correct subtraction
Language	<u>Task 1</u> Examiner will read out two sentences and subject is to repeat the sentences accurately.	<u>Task 1</u> Score of 1 is given for each correctly read sentence; a range of score from 0 to 2 can be awarded.
	<u>Task 2</u> Subject is tasked to name words that begin with a specific letter in one minute.	<u>Task 2</u> A maximum score of 1 is given if subject can name more than 11 words.
Abstraction	Subject is to name the similarity between the following pair of items: train – bicycle and watch – ruler	Score of 1 is given for each correct pair; a range of score from 0 to 2 can be awarded.
Delayed Recall	Subject is to recall the 5 words previously read out in the Memory test without any prompting or reminders from the examiner.	Score is given based on the number of correct responses; a range of score from 0 to 5 can be awarded.
Orientation	Date, month, year, day, place and city	Score of 1 is given for each correct response; a range of score from 0 to 6 can be awarded.